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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/606,569	06/29/00	BIGAZZI	M 67206

HM12/0404

MCGLEW AND TUTTLE P C
SARBOROUGH STATION
SCARBOROUGH NY 10510-0827

EXAMINER	
DEBERRY,R	
ART UNIT	**PAPER NUMBER**
1647	5

DATE MAILED: 04/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/606,569	BIGAZZI, MARIO	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-6* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

Status of Application, Amendments and/or Claims

Applicant's election of Group I (claims 1-5) in Paper No. 4 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claim 6 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 4.

Drawings

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed. If the filed drawings are formal drawings, please indicate as such in response to this Office action and the drawings will be reviewed by the draftsman. New matter may not be introduced when making drawing corrections.

Objection to Specification

The disclosure is objected to because of the following informalities: The figures are unclear. In figure 2, it is not clear what N.1 and N.2 represent. In figure 3, it is not clear if N.1 represents 1 and N.2 represents 2. In figure 4, is RLX present in the lower lanes of each panel or in the lower panel? If RLX is present in the lower lanes as stated in the specification, it is not clear what the lower panel represents. Do lanes 1-6

represent different clones? It is not clear what the asterisk represents. Appropriate correction is required.

Sequence Rules

The instant application fails to fully comply with the sequence rules 37 CFR 1.821-1.825 because each disclosure of a sequence embraced by the definitions set forth in the rules fails to refer to the required sequence identifier (SEQ ID NO:). This occurs on page 10, lines 3-4. Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-28 of U.S. Patent No. 5,952,296 (cited in the IDS) in view of Piccinni *et al.* In U.S. Patent No. 5,952,296,

claims 20-28 are drawn to a method of treating a condition deriving from the release of histamine involving allergic rhinitis, bronchial asthma, anaphylactic disease, pharmacological allergy, alteration in tissue reaction, or inflammation sustained by the release of histamine, in a human patient exhibiting said condition, comprising administering to said patient an effective amount of relaxin or derivative thereof for preventing said release of histamine for relieving said rhinitis, for relieving said asthma, for relieving said anaphylactic disease, for relieving said pharmacological allergy, for relieving said alteration in tissue reaction, or for reducing or inhibiting said inflammation.

Although the conflicting claims are not identical, they are not patentably distinct from each other. Mast cells secrete histamine when triggered by the binding of IgE antibodies. Th2 plays a triggering role in the activation and/or recruitment of IgE antibody-producing B cells, mast cells, and eosinophils (the cellular triad involved in the allergic inflammation) (Piccinni *et al.*). Therefore, Th2 is involved in triggering the release of histamines involved in the conditions listed in the claims of U.S. Patent No. 5,952,296. In the instant application, the claims are drawn to a method of treating a Th2-dominated disease in a human patient exhibiting said disease, a method of inhibiting a pathogenic Th2 response in a human patient exhibiting said pathogenic Th2 response, a method of stimulating the development of activated human T cells into Th1-like effectors for treating a Th2-dominated disease in a human patient exhibiting said disease, a method of treating a Th2-dominated disease in a human patient exhibiting said disease and method of treating a Th2-dominated disease in a human patient exhibiting said disease all of the above methods comprising administering to the patient

an effective amount of relaxin or a derivative thereof. Th1 cells produce interferon (IFN)-γ. IFN-γ and relaxin play a negative regulatory role on the development of Th2 cells (Piccinni *et al.*). Since the species claims of U.S. Patent No. 5,952,296 are encompassed by the genus claims of the instant application, the species renders the genus obvious.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for relaxin, does not reasonably provide enablement for derivatives of relaxin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification teaches relaxin as a 6-kDa polypeptide hormone predominantly produced by the corpus lutem during pregnancy. However, the specification does not teach how to make any derivative of relaxin and provides no assay to evaluate the function of any modified polypeptide. In addition the specification does not disclose a definition of what is meant by a derivative of relaxin. A derivative could mean a mutation, deletion, substitution and/or addition of a nucleotide or a residue. A derivative could also denote pegylation, glycosylation or

other post-translational modifications. Absent any means to assess the function of the polypeptide, it would require an indeterminate quantity of fundamentally unpredictable investigational experimentation of the skilled artisan to determine whether any modified polypeptide could be used in the same manner as the native exemplar. Such experimentation would be undue for one skilled in this art.

Furthermore, in order to make a sequence derivative/variant, for example, with the reasonable assurance that it would have the desirable properties of the invention, the artisan would need to know which regions of the disclosed polypeptide are responsible for the interactions underlying its biological function(s). As is well recognized in the art, any modification (even a "conservative" substitution) to a critical structural region of a protein is likely to significantly alter its functional properties. The disclosure provides no guidance as to which regions of the protein would be tolerant of modification and which would not, and it provides no working example of any variant sequence which would be within the claims. It is in no way predictable that randomly selected mutations, deletions, *etc.* in the disclosed sequence would afford a protein having activity comparable to the one disclosed.

For the reasons discussed above, such experimentation would be undue for one skilled in this art. In this connection, the Board and the Federal Circuit have held in several instances that the disclosure of a single amino acid sequence is not sufficient to enable claims directed to any functionally equivalent variants of that sequence. See, for example, *Ex parte Maizel,* 27 USPQ2d 1662 (BPAI 1993).

Due to the large quantity of experimentation necessary to make derivatives of relaxin and assess the function, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to same, and the unpredictability of the effects of mutation on protein structure and function, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification provides adequate written description for relaxin, but no variants. Claims 1-5 are directed to methods of using relaxin or derivatives thereof.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of relaxin, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only relaxin, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A derivative of relaxin is indefinite because it is not clear whether a derivative suggests a mutation, deletion, substitution and/or addition of a residue or nucleotide or other modifications. The metes and bounds cannot be determined from the claims. The claims do not convey to the skilled artisan the minimal structural and functional requirements of relaxin to satisfy the limitations.

The terms "Th2-dominated disease" and "pathogenic Th2 response" are indefinite because clear and concise definitions of what these conditions encompass were never disclosed in the specification.

Conclusion

No claims are allowed.

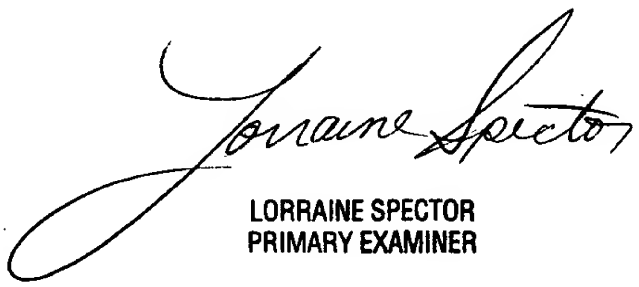
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on Mondays-Fridays 8:00 a.m. - 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 308-2742 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD

RMD
April 3, 2001



LORRAINE SPECTOR
PRIMARY EXAMINER